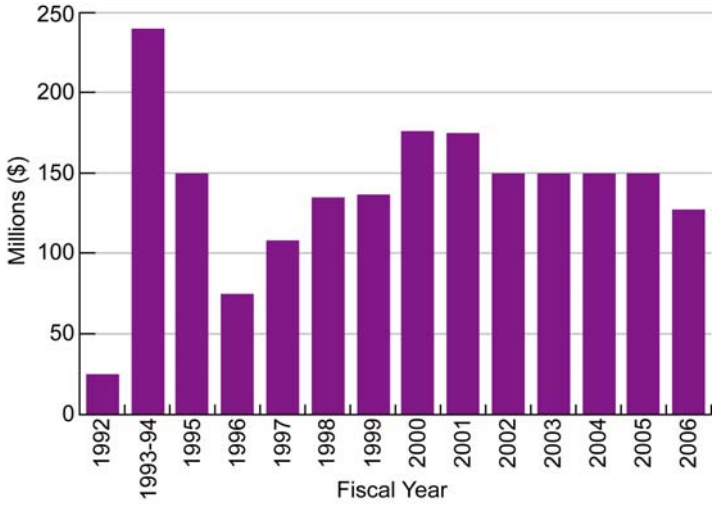
Congressionally Directed Medical Research Programs
Breast Cancer Research Program

History

Grassroots efforts by the breast cancer advocacy community led to congressional appropriations to the Department of Defense (DOD) of $25 million (M) in Fiscal Year 1992 (FY92) and $210M in FY93 for breast cancer research. This enabled the development of a unique partnership among the public, Congress, and the military. The Congressionally Directed Medical Research Programs (CDMRP) was created within the U.S. Army Medical Research and Materiel Command (USAMRMC) in FY93 to manage the Breast Cancer Research Program (BCRP). Funds for the BCRP are added to the DOD budget by Congress (generally as Defense Health Program [Research, Development, Test, and Evaluation]). The BCRP is conducted according to the two-tier review model recommended by the National Academy of Sciences Institute of Medicine; this model has received high praise from the scientific community, advocacy groups, and Congress.



Unique Features of the BCRP

Consumer Advocate Participation

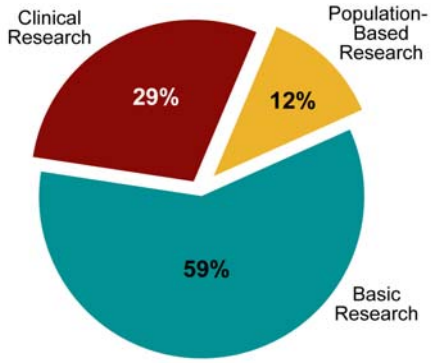
As active members of the BCRP, consumer advocates participate in setting program priorities and making funding decisions. Over 400 consumer advocates have served on peer and programmatic review panels for the BCRP since 1993. Consumer advocates' firsthand experience with breast cancer provides a unique perspective that is complementary to the scientific expertise. This perspective helps the scientists understand the human side of how the research will impact the community and allows for funding decisions that reflect the concerns and needs of patients, the clinicians who treat them, and survivors and their families. An additional benefit is that consumer advocates take what they have learned back to their communities. This results in increased awareness of the importance of research and a stronger relationship between the scientific community and the consumer advocate community. The overwhelming success of the BCRP precedent for including consumer advocates in the review process has influenced other funding agencies to follow suit.

"As a result of this experience, I feel more empowered… I understand the importance of funding breast cancer research. I understand the role consumers play in the review process. I am more aware of the things I can do to promote good health. …I feel better equipped to continue my breast cancer advocacy work. I will encourage other breast cancer survivors to become consumer reviewers. It is a life changing experience." *Ethel Nettelsbay Consumer Peer Reviewer, BCRP*

Filling Gaps

The BCRP fills important gaps not addressed by other funding agencies in support of breast cancer research. The BCRP vision is adapted yearly to facilitate rapid change and to better target funding to the most critical research areas, thus ensuring that the program remains responsive to current needs and future opportunities. A highly flexible management process with proven stewardship, well-qualified people, and productive partnerships is key to the BCRP's success.

Investment Strategy



BCRP Portfolio

BCRP Vision: to eradicate breast cancer

The overall goal of the BCRP is to promote research focused on eradicating breast cancer. The BCRP focuses its funding on innovative projects, particularly those involving multi-disciplinary and/or multi-institutional collaborations and alliances that have the potential to make a significant impact on breast cancer. Projects that address underinvestigated avenues of research or novel applications of existing technologies are strongly encouraged. Within this context, the BCRP seeks to fund a balanced portfolio of scientifically meritorious research on the prevention, detection, diagnosis, and treatment of breast cancer.

Innovative Award Mechanisms

The BCRP seeks to fund innovative and groundbreaking research by encouraging thinking "outside the box" and fostering creative collaborations. Unlike traditional awards, preliminary data are not a requirement for many BCRP award mechanisms.

- Idea Awards/Synergistic Idea Awards
  No preliminary data required; encourage innovative, novel approaches
- Concept Awards
  Fund initial untested theories that could give rise to testable hypotheses
- Innovator Awards/Era of Hope Scholar/Era of Hope Postdoctoral Awards
  Provide visionary investigators at different career stages with the funding and freedom to pursue creative, potentially breakthrough research

- Clinical Translational Research Awards
  Foster the translation of new discoveries from bench to bedside
- Center of Excellence Awards
  Engage expert consumers, scientists, and clinicians from multiple disciplines to establish centers focusing on innovative breast cancer research
- Multidisciplinary Postdoctoral Awards
  Encourage development of research expertise in several diverse disciplines to enhance the training of future leaders in the field of breast cancer research

BCRP Research Highlights (FY93–Present)

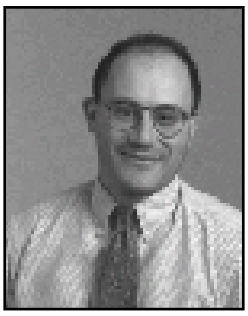
The BCRP is advancing the quality of care for breast cancer by funding innovative research, facilitating collaborative connections, supporting development of research resources, and training the clinical care providers and researchers of the future.

Notable Research Advances

- Synthesized a carrier-tagged analog of curcumin that is tenfold more potent than cisplatin in killing breast cancer cells
- Instrumental in the development of the breast cancer therapeutic agent Herceptin®
- Generated a vaccine targeted against ductal carcinoma in situ
- Developed a novel laser treatment for small, localized breast cancer tumors as a less invasive alternative to lumpectomy
- Numerous new research resources generated—antibodies, cell lines, animal models, expression vectors, repositories, databases, computer models, etc.

Individual Success Stories

CONCEPT AWARDS provide investigators at all levels with the initial funding necessary to carry out preliminary testing of innovative and untested ideas, often allowing the generation of preliminary data that can be used to secure more long-term funding.



Dr. Dennis Sgroi, Massachusetts General Hospital, has examined the levels of expression of certain genes in breast cancer as a way of identifying prognostic categories that may guide cancer treatment choices. In a recently published study, Dr. Sgroi and his colleagues performed genome-wide microarray analysis on 60 tumor samples taken from patients who had received tamoxifen treatment for early-stage, estrogen receptor-positive (ER+) breast cancer. This study revealed that the ratio between the expression levels of two genes, HOXB13 and IL17BR, was a strong predictor of tumor recurrence. High levels of HOXB13 or low levels of IL17BR expression suggested that tamoxifen therapy would fail. These studies need to be validated in a larger population; however, it appears that this simple test will assist oncologists in deciding whether to use tamoxifen therapy or an alternative therapy in treating ER+ breast cancer patients.

- *Ma XJ, Wang Z, Ryan PD, et al. 2004. A two-gene expression ratio predicts clinical outcome in breast cancer patients treated with tamoxifen.* Cancer Cell 5:607–616.

INNOVATOR AWARDS fund accomplished, creative individuals with a history of innovation and visionary leadership within their fields, allowing them the freedom to pursue their most innovative plans that could ultimately lead to the eradication of breast cancer.

Dr. Erkki Ruoslahti, The Burnham Institute, is developing a tumor targeting strategy that concentrates therapeutic agents directly in and around tumor tissues by making use of the unique features of the vascular system. Dr. Ruoslahti has used libraries of phage-displayed peptides to identify specific markers of tumor vasculature, the vasculature of pre-malignant lesions, and of tumor lymphatics. The homing peptides he discovered have shown promise in targeting drugs specifically to stop the growth of breast tumors and prevent metastasis. An additional benefit of this type of targeted therapy is the potential for alleviating the toxic side effects associated with many therapeutic cancer agents.

Dr. Judah Folkman, Children's Hospital Boston and Harvard Medical School, has accumulated substantial evidence for his hypothesis that microscopic tumors can be held in check by a molecular switch that turns on angiogenesis. Dr. Folkman showed that in mice bearing different types of human cancer, specific angiogenic proteins produced by a tumor are taken up by platelets and sequestered. Analysis of the "platelet angiogenic profile" can detect an early microscopic tumor as small as 1 cubic millimeter, offering exciting possibilities for early cancer detection. The corollary to detecting tumors at this early stage is that treatment with angiogenesis inhibitors could prevent the development of cancer from these microscopic tumors essentially, turning cancer into a "chronic manageable disease" in Dr. Folkman's words.

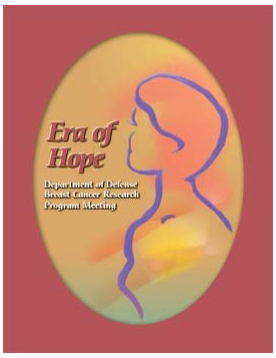
ERA OF HOPE SCHOLARS are exceptionally talented, early-career scientists who have demonstrated that they are the "best and brightest" in their fields through their extraordinary creativity, vision, and productivity.

Dr. Vera Donnenberg, University of Pittsburgh, has made great strides in her studies of breast cancer stem cells in less than a year after receiving her award.
Dr. Donnenberg has identified and isolated breast cancer stem cells by adapting an assay that works with small numbers of cells. She has discovered that stem cells are as resistant to chemotherapy as their normal tissue counterparts and is investigating mechanisms of multidrug resistance (MDR) in these cells.

Dr. Geoffrey Chang, Scripps Research Institute, has also enjoyed extraordinary success in the short time since receiving his award. Dr. Chang is exploring a novel area of research by integrating structure, function, and chemistry in the discovery and design of MDR reversal agents. His goal is to identify new classes of inhibitor compounds that could reverse MDR in breast cancer. Dr. Chang stated that without this grant, he would be unable to pursue this research.

The success of these two exceptional young scientists is being compounded by a collaboration formed after they met at a luncheon sponsored by the BCRP. As a result, Dr. Donnenberg will use her assay to evaluate the new MDR reversal agents created by Dr. Chang.

Success in Support of Collaboration



ERA OF HOPE MEETINGS are major international events held every 2 years that include all investigators funded by the BCRP and other leading scientists and physicians in the field, breast cancer survivors and advocates, policymakers, and the general public. These meetings, which serve as forums for free and active interchange of ideas among investigators of diverse disciplines, often result in collaborations among investigators or spawn new research ideas.

CENTER OF EXCELLENCE (COE) AWARDS support synergistic, multidisciplinary, and multi-institutional research efforts that address a single, overarching problem critical to the prevention, detection, diagnosis, and/or treatment of breast cancer. Breast cancer consumer advocate/survivor groups play an active and integrated role in every aspect of these COEs.

Benign Breast Disease: Toward Molecular Prediction of Breast Cancer Risk

(Principal Investigator: Dr. Lynn Hartmann, Mayo Clinic and Foundation) The goal of this COE is to improve breast cancer risk prediction for women with benign breast disease (BBD) by establishing a tissue repository from a retrospective cohort of women with BBD and using this repository to discover and assess biomarkers of breast cancer risk. To date, the investigators have found that BBD is a common, heterogeneous event associated with a long-term (>30 yr) increased risk of breast cancer. Furthermore, they have shown that BBD represents a valid platform for testing molecular markers of breast cancer risk and also can be used to develop multivariate risk prediction models. Improved identification of women at significantly increased risk enables better development of surveillance and risk reduction strategies. Moreover, discovering new biomarkers in BBD may help to identify causative pathways in breast carcinogenesis that could then be targeted through specific prevention strategies.

- *Hartmann LC, Sellers TA, Frost MH, et al. 2005. Benign breast disease and breast cancer risk.* New England Journal of Medicine *353:229–237.*

Blueprint for Regional Excellence in Breast Cancer Care

(Principal Investigator: Dr. Laura Esserman, University of California, San Francisco) The goal of this COE is to improve the quality of breast cancer care by integrating the most relevant research knowledge and using it to tailor treatment to biology, patient preference, and performance. Current standard of care recommendations involve treatment of breast cancer patients with some standard combination of surgery, radiation, and systemic therapy, rarely taking into account individualized data. The researchers involved in this COE have begun to approach this problem by creating an information systems supported framework to facilitate optimal therapeutic decisions and provide valuable feedback. They designed and built a networking system to support solutions with scalable, open architecture and provide both patients and clinicians with timely decision support at the point of care. This undertaking will serve as a prototype for ongoing regional and national efforts to improve breast cancer outcomes. Combining the power of informatics with expertise in management science and breast cancer may provide a dramatic improvement in the quality of service and treatment of patients that can be scaled to other providers and health care delivery areas.

- *Ozanne EM and Esserman LJ. 2004. Evaluation of breast cancer risk assessment techniques: A cost-effectiveness analysis.* Cancer Epidemiology Biomarkers and Prevention *13:2043–2052.*

BIOTECHNOLOGY CLINICAL PARTNERSHIP AWARDS facilitate partnerships between biotechnology industry and academic institutions to reduce the challenges related to drug development and accelerate the delivery of novel breast cancer therapeutics and chemopreventives.

Wilex AG, a German-based biopharmaceutical company, and Fox Chase Cancer Center received the first Biotechnology Clinical Partnership Award in FY02 to develop and test WX-UK1, a breast cancer antimetastatic agent. WX-UK1 is a serine proteinase inhibitor that impairs tumor growth and metastasis in a rat model of breast cancer. WX-UK1 disrupts the activity of a biological target that is directly connected to cancer progression, offering a new mechanism of action—the prevention of metastasis. Through this award, WX-UK1 received Investigational New Drug status from the U.S. Food and Drug Administration. In addition, a Phase 1 clinical trial to evaluate the safety of this drug was completed. Results indicate that WX-UK1 is well tolerated. Recruitment of patients for a Phase 2 trial is in progress.

Translational Research Highlights

- Clinical and Experimental Therapeutics – (Dr. Mark Pegram) This study demonstrated the potential for combining Herceptin® (anti-Her2) therapy with Avastin® (antivascular endothelial growth factor) to increase effectiveness of treatment.

  Currently in Phase 2 clinical Trial

- Sentinel Lymph Nodes – (Dr. Kathryn Verbanac) The study demonstrated and confirmed that sentinel lymph nodes are indicators of metastatic progression of disease.

  Currently a Standard of Care

- Immunotherapy – (Dr. Daniela Santoli) The researchers demonstrated that TALL-104 cells were able to selectively kill cancer cells. Their greatest potential was identified as an adjuvant therapy for cancer cells.

  Currently in human clinical trials in Europe

- Detection and Diagnosis – (Dr. Stephen Bown) The team constructed and established two techniques: optical biopsy for diagnosis and interstitial laser photocoagulation for treatment.

  Currently under development at Optimum Technologies, Inc.

- Detection and Diagnosis – (Dr. Daniel Kopans) The team studied a digital tomosynthesis system for imaging.

  General Electric has invested in its development and expects it in the clinic in 2 years

- Primary Prevention, Nutrition – (Dr. Henry Thompson) The investigators determined the effects of increased fruit and vegetable intake on oxidative DNA base damage and lipid peroxidation in a population of women at elevated risk for breast cancer.

  Subjects completed the dietary intervention – increased intake of fruit and vegetables decreased oxidative DNA damage

http://cdmrp.army.mil/bcrp